FEB - 5 2014

510(k) Summary of Safety and Effectiveness for the

ADVIA® Centaur Intact Parathyroid (iPTH) Assay

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

A. 510(k) Number: k133601

B. Date of Preparation: February 4, 2014

C. Proprietary and Established Names:

ADVIA® Centaur Intact Parathyroid Hormone (iPTH) Assay

D. Applicant:

Siemens Healthcare Diagnostics Inc.,
511 Benedict Ave, Tarrytown, NY 10591
Philip Liu, Ph.D.
Senior Manager, Regulatory Affairs and Compliance
Office: (914) 524-2443
Fax: (914) 524-3579

E. Regulatory Information:

1. Regulation section: 21 CFR § 862.1545
2. Classification: Class II
3. Product Code: CEW, Parathyroid Hormone Test System
4. Panel: Clinical Chemistry

F. Predicate Device:

The ADVIA® Centaur Intact Parathyroid Hormone (iPTH) Assay using the ADVIA Centaur XP was cleared under 510(k) k121981. The assay is also being marketed on the instrument family member, ADVIA Centaur, following FDA's *Replacement Reagent and Instrument Family Policy* (December 11, 2003).

G. Intended Use / Indications for Use:

The ADVIA Centaur iPTH assay is for *in vitro* diagnostic use in the quantitative determination of intact parathyroid hormone (iPTH) in EDTA plasma or serum using the ADVIA Centaur and ADVIA Centaur XP systems. This assay is intended to be used to aid in the differential diagnosis of hyperparathyroidism and hypoparathyroidism.

H. Device Description:

The ADVIA Centaur iPTH assay is a two-site sandwich immunoassay using direct chemiluminometric technology, which uses constant amounts of an antihuman PTH antibody in the Lite Reagent and an antihuman PTH antibody in the Solid Phase Reagent. The first antibody is a polyclonal goat antihuman PTH (N-terminal 1-34) antibody labeled with acridinium ester. The second antibody is a biotinylated polyclonal

goat antihuman PTH (39-84 region) antibody that is preformed to streptavidin coated paramagnetic latex particles in the Solid Phase reagent.

The ADVIA Centaur iPTH reagent kit contains the following:

- ReadyPack® primary reagent pack containing ADVIA Centaur Lite and Solid Phase Reagent)
- ADVIA Centaur iPTH Master Curve card

Materials Required but Not Provided

- iPTH Calibrator

Optional Reagents

- ADVIA Centaur Multi-Diluent 11
- iPTH 1, 2, 3 quality control material
- iPTH Master Curve Material

I. Description of Device Modification

The modification to the ADVIA Centaur iPTH assay is due to the qualification of new polyclonal goat anti-human PTH antibody pools:

- Newly qualified pool for polyclonal goat anti-human PTH N- terminal antibody (Lite Reagent) produced by Siemens (Elkhart).
- Newly qualified pool for polyclonal goat anti-human PTH C- terminal antibody (Solid Phase Reagent) produced by Siemens (Elkhart).

J. Comparison of Predicate Device and Modified Device:

The following table provides a comparison between the Predicate ADVIA Centaur iPTH assay (with the current polyclonal antibody pools) and the modified ADVIA Centaur iPTH assay with the newly-qualified polyclonal antibody pools.

Item	Modified Device: ADVIA Centaur Intact PTH Assay	Predicate Device: ADVIA Centaur Intact PTH Assay
Intended Use	For *in vitro* diagnostic use in the quantitative determination of intact parathyroid hormone (iPTH) in EDTA plasma or serum using the ADVIA Centaur* and ADVIA Centaur XP systems	Same * ADVIA Centaur was added after clearance following the guidelines of the FDA's Replacement Reagent and Instrument Family Policy
Indications for Use	This assay is intended to be used to aid in the differential diagnosis of hyperparathyroidism and hypoparathyroidism.	Same
Sample type	EDTA Plasma, Serum	Same
Measurement	Quantitative	Same
Operating Principle	Sandwich immunoassay	Same
Technology	Chemiluminescence	Same
Detection Antibody	Goat polyclonal antibody conjugated to Acridium Ester	Same

Item	Modified Device: ADVIA Centaur Intact PTH Assay	Predicate Device: ADVIA Centaur Intact PTH Assay
Capture Antibody	Goat polyclonal antibody conjugated to biotin directly coupled to streptavidin magnetic particles	Same
Assay Range	6.3 – 1900 pg/mL	5.5 – 1900 pg/mL
Sample Volume	200 µL	Same
Calibrators	Siemens iPTH Calibrators	Same
Calibration	2 Point	Same
Number of calibrators	Two (2) levels	Same
Expected Values	13.8 – 85.0 pg/mL (plasma) 12.4 – 76.8 pg/mL (serum)	Same

K. Standard/Guidance Document Referenced:

- CLSI Guideline EP5-A2: Evaluation of Precision Performance of Qualitative Measurement Methods
- CLSI Guideline EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures
- CLSI Guideline EP6-A: Evaluation of the Linearity of Qualitative Measurement Methods
- CLSI Guideline C28-A3c: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline
- CLSI Guideline EP7-A2: Interference Testing in Clinical Chemistry; Approved Guideline
- Medical devices – Application of risk management to medical devices (ANSI/AAMI/ISO 14971:2007/(R) 2010)

L. Performance Characteristics

Substantial equivalence was demonstrated by testing several performance characteristics including imprecision, interfering and cross-reacting substances, and method comparison.

a. Precision

Precision was evaluated following CLSI guideline EP5-A2. Two replicates of each of 7 samples including 4 EDTA plasma pools and 3 levels of commercial control materials were assayed in duplicate over the course of 20 days, on 2 instruments using 2 lots of reagent, two runs per day, for a total of 40 runs and 80 replicates. A representative lot is summarized below:

Sample	MEAN (pg/mL)	Within Run %CV	Total %CV
Pool 1	16.1	7.1	7.7
Control 1	38.7	3.6	4.7
Pool 2	62.8	2.7	3.7
Control 2	185	2.4	3.2
Control 3	663	2.2	2.8

Sample	MEAN (pg/mL)	Within Run %CV	Total %CV
Pool 3	839	3.0	3.9
Pool 4	1698	2.3	3.2

b. Detection Limits

The Limit of Blank (LoB), Limit of Detection (LoD), and the Limit of Quantitation (LoQ) were estimated per CLSI EP17-A2. The LoB was calculated non-parametrically. The LoQ was estimated as the dose corresponding to 20% Total CV using the precision profile method.

A single experimental design was used to generate the data for LoB, LoD and LoQ. Multi-Diluent 11 (assay specific diluent) was used as the blank. Five test samples were prepared by spiking analyte into diluent and/or diluting plasma samples to obtain the following approximate concentrations: 1, 2, 5, 10, and 15 pg/mL. These samples were tested at n=6 x 2 instruments x 5 days for a total of n=60 per reagent lot (2 reagents lots were used).

The results are as follows:

LoB	LoD	LoQ
0.1 pg/mL	2.7 pg/mL	6.3 pg/mL

c. Linearity / Assay Range

Linearity across the assay range was evaluated following the guidelines of CLSI EP6-A. Twelve test concentrations (pools) ranging from 4.4 to 2021 pg/mL were prepared by dilution of high and low concentration pools. Testing of the pools across the assay range was done with one reagent lot.

The regression statistics (Observed vs. Expected Values with weighed linear fit) for the linearity study were as follows:

$y = 0.98x - 4.98$, $R = 1.00$

d. High Dose Hook Effect

High dose hook effect was tested. A hook sample was prepared by spiking iPTH stock into diluent to achieve a concentration of approximately 144,000 pg/mL. The hook sample was tested in triplicate with 2 reagent lots. No high dose hook was observed for either reagent lot.

e. Interfering Substances

Interference by hemoglobin, triglycerides, bilirubin, and biotin was evaluated using two patient plasma pools with endogenous iPTH concentrations of ~20 pg/mL and ~200 pg/mL. There was no indication of interference ($\leq$ 10% effect) up to the interferent levels claimed.

Interfering Substance	Conc.	Test Sample (pg/mL)	Control Sample (pg/mL)	% Bias
Hemoglobin	500 mg/dL	30.9	29.6	4%
		203	204	-1%
Triglycerides	3000 mg/dL	27.4	25.7	7%
		153	148	-4%
Conjugated Bilirubin	40 mg/dL	31.8	29.8	7%
		212	211	0%
Unconjugated Bilirubin	40 mg/dL	24.1	22.5	7%
		197	183	8%
Biotin	1000 ng/mL	32.6	30.0	8%
		222	236	6%

f. Cross reacting Substances

Cross reactivity was evaluated using a plasma sample with endogenous iPTH and an assay specific Multi-diluent 11 (buffered goat serum with **no analyte**). No cross reactivity was observed at the highest levels tested with the exception of the PTH 7 – 84 fragment (~ 51%).

Cross reactant	Conc. (pg/mL)	Multi-Dil 11 IPTH Dose (pg/mL)	%Cross Reactivity	iPTH Dose (pg/mL)	%Cross Reactivity
PTH 1-34	300	0.0	-0.2	33.9	0.1
PTH 39-68	100,000	0.1	0.0	22.2	0.0
PTH 39-84	100,000	2.7	0.0	17.5	0.0
PTH 44-68	100,000	0.0	0.0	23.4	0.0
PTH 53-84	100,000	2.0	0.0	27.1	0.0
Calcitonin	100,000	0.0	0.0	33.1	0.0
PTH 7-84	300	130	33	192	51
Beta-Cross Laps	1000	0.5	0.0	35.8	0.2
Osteocalcin	50,000	0.2	0.0	34.7	0.0

g. Method Comparison

Method Comparison studies were done with 106 unaltered native matched serum and plasma samples to demonstrate equivalence to the Predicate (ADVIA Centaur iPTH assay). The ADVIA Centaur iPTH assay shows good correlation in sample results compared to the Predicate.

System (y)	N	Regression Equation*	R**	Sample Range (pg/mL)
ADVIA Centaur iPTH (EDTA Plasma)	106	y = 0.98x + 10.6	1.00	11.8 - 1862
ADVIA Centaur iPTH (Serum)	105***	y =1.00x + 5.0	1.00	9.8 - 1868

x =Predicate (ADVIA Centaur iPTH Assay)

* Passing & Bablok

** Least Squares Linear regression

*** Sample outside of assay range was excluded

h. Expected Values

The reference range of the Predicate was verified following the guidelines of CLSI C28-A3c. Forty (40) plasma and 40 serum samples obtained from apparently healthy individuals (calcium and inorganic phosphorus results within their respective reference ranges) were tested using 2 reagent lots across 4 instruments. The results are as follows:

	%Within Range			
	Plasma		Serum	
Range	Lot 1	Lot 2	Lot 1	Lot 2
12 – 85 pg/mL	100.0%	100.0%	97.5%	95.0%

i. Stability

The on board stability of the reagent is 28 days with a calibration interval of 14 days. The ADVIA Centaur Intact PTH assay reagent is stable until the date printed on the label when stored at 2-8°C.

M. Conclusions

Comparative testing of the modified ADVIA Centaur iPTH assay is substantially equivalent in principle and performance to the Predicate Device, ADVIA Centaur Intact PTH assay, cleared under 510(k) k121981.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

February 5, 2014

SIEMENS HEALTHCARE DIAGNOSTICS INC.
DR. PHILIP LIU
SENIOR MANAGER, REGULATORY AFFAIRS
511 BENEDICT AVE.
TARRYTOWN NY 10591

Re: K133601
Trade/Device Name: ADVIA Centaur Intact Parathyroid Hormone (iPTH) Assay
Regulation Number: 21 CFR 862.1545
Regulation Name: Parathyroid hormone test system
Regulatory Class: II
Product Code: CEW
Dated: December 30, 2013
Received: December 31, 2013

Dear Dr. Liu:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement on last page.

510(k) Number *(if known)*
k133601

Device Name
ADVIA Centaur® Intact Parathyroid Hormone (iPTH) assay

Indications for Use *(Describe)*

The ADVIA® Centaur Intact Parathyroid (iPTH) assay is for in vitro diagnostic use in the quantitative determination of intact parathyroid hormone (iPTH) in EDTA plasma or serum using the ADVIA Centaur and ADVIA Centaur XP systems. This assay is intended to be used to aid in the differential diagnosis of hyperparathyroidism and hypoparathyroidism.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Yung W. Chan -S

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